REMARKS

Applicant respectfully requests reconsideration. Claims 100-107 were previously pending in this application. Claims 100-102 have been amended herein. Claim 103 has been canceled without prejudice or disclaimer. As a result, claims 100-102 and 104-107 are still pending for examination, with claims 100 and 105-107 being independent claims. No new matter has been added.

Applicant acknowledges and thanks the Examiner for the withdrawal of the previous objection and rejections. The remaining objection and rejections are addressed below.

Finality of the Office Action

Applicant disagrees with the finality of the Office Action. Initially it is noted that the body of the Office Action never refers to the action being a Final Office Action. No reason has been provided by the Office for asserting that the Office Action is a Final Office Action. The only place in the Office Action that refers to a Final Action is on the Summary Page, where the Final Action box is checked. The Office Action itself indicates that all the prior rejections have been withdrawn and that new rejections have been made. It is Applicant's understanding that the Office Action was designated as a Final Office Action on the Summary Page in error. It is requested that the Finality of the Action be withdrawn.

Sequence Requirements

The Examiner pointed out that claims 101 and 102 did not comply with the rules of 37 C.F.R. §§ 1.821-1.825 because the claims did not include corresponding SEQ ID NOs. Applicant, in response, has amended the claims to recite the SEQ ID NOs. The amended claims are now believed to be in full compliance with the sequence rules.

Rejections Under 35 U.S.C. § 112

Claims 100-104 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner pointed out that the length limitation of 16-40

nucleotides recited in claims 100 and 105 was rendered indefinite because the oligonucleotide of SEQ ID NO:313 is 24 nucleotides in length. As discussed below, Applicant traverses in part.

In order to advance prosecution, Applicant has amended claim 100 to limit the length of the oligonucleotide to "24-40." It is believed that the amendment is unnecessary because the sequence of the oligonucleotide effectively limited the minimal length of the oligonucleotide to 24 nucleotides. Thus the amendment to the claim does not narrow the scope of the claim.

The Office also asserts that claim 105 recites a length limitation of 16-40 nucleotides in length. Applicant disagrees. Contrary to the allegation, claim 105 does not recite the limitation of 16-40 nucleotides in length. Rather, claim 105 recites "...wherein the oligonucleotide is *24 nucleotides in length*." Therefore, the claim is definite.

Accordingly, it is respectfully requested that the rejections made under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 100-107 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable in view of Krieg et al. (WO01/22972A2), April 5, 2001 and Samani et al. (Antisense and Nucleic Acid Drug Development 2001 Vol. 11 pgs. 129-136). According to the Examiner, the cited publication by Krieg et al. teaches sequence 343s which corresponds to SEQ ID NO: 313 and that the disclosure of Krieg et al. teaches a chimeric oligonucleotide comprising an internal phosphodiester internucleotide linkage, thereby rendering the instant claims obvious. Applicant respectfully disagrees.

WO01/22972A2 (Krieg et al) discloses T rich ODN which optionally have CpG dinucleotides. The ODN may be fully phosphodiester or phosphorothioate or may have a chimeric backbone. The invention described in Krieg et al. is based in part on the discovery that nucleic acid sequences which did not contain CpG motifs were immunostimulatory, and that those which have chimeric backbones have unexpectedly enhanced immune stimulating properties. Indeed, in the relevant sections of the Krieg publication where chimeric oligonucleotides of the invention are described, it expressly teaches that the immunostimulatory center motif (shown as "Z") does not include a CG (See, for example, second full paragraph on page 8 as published). Krieg et al. teaches

that SEQ ID NO. 343 is a fully phosphorothioate oligonucleotide, not a chimeric oligonucleotide. As noted by the Examiner, this sequence is listed in Table A of the Krieg publication.

The Examiner argued that the instant claims are rendered obvious by Krieg et al. because Krieg et al. teach that a chimeric combination of phosphodiester and phosphorothioate oligonucleotide is preferable over a fully modified oligonucleotide. However, this notion is provided in the context of *plasmid vectors*, that is, cells' ability to take up a plasmid vector containing completely phosphorothioate nucleic acid. Applicant contends that this is taken out of context in the rejection of the instant claims, because the instant invention teaches a chimeric oligonucleotide of up to 40 nucleotides in length and does not pertain to a plasmid vector.

The Examiner also cited Samani et al. for the proposition that "...oligonucleotides with a minimum of phosphorothioate linkages [are] well known in the art" and that phosphodiesters are rapidly degraded (Page 6, Office Action). According to the Office the skilled artisan would have placed a phosphodiester between the C and G to produce an oligonucleotide with a CpG that has a phosphodiester internucleotide linkage and stabilized internucleotide linkages based on the teachings of Krieg et al. Applicant disagrees.

There is no disclosure in either cited reference concerning specifically sited phosphodiester or phosphodiester-like internucleotide linkages in any immunostimulatory nucleic acid, as claimed in the instant application. The general disclosure in Krieg et al of chimeric backbones does not clearly disclose the instantly claimed specifically sited phosphodiester or phosphodiester-like internucleotide linkages. Samani et al does not provide the skilled artisan any further guidance on selecting the site to place the phosphodiester internucleotide linkage. The inventors have discovered surprising advantages associated with the specific placement of phosphodiester and/or phosphodiester-like internucleotide linkages between C-G dinucleotides. It would not have been obvious to a skilled person to modify only those particular locations, out of all the possible locations that could be modified, in order to arrive at the instantly claimed invention. The cited references provide no guidance for selecting the specifically claimed site to place the phosphodiester internucleotide linkage.

Further the skilled artisan would not have reasonably expect, on the basis of the teachings of the cited references, that such modifications would in fact result in immunostimulatory nucleic acids

with improved potency and/or reduced toxicity as compared to fully stabilized immunostimulatory nucleic acids. It was discovered surprisingly according to the invention that such nucleic acids have at least similar immunostimulatory or even better immunostimulatory activity than nucleic acids that have complete phosphorothioate internucleotide linkages. It was expected that the modified nucleic acids of the invention might have less activity because they would be more susceptible to breakage at the key active sites between purine and pyrimidine molecules. These teachings are found in the specification at least on page 33 lines 11-24.

Accordingly, Applicant respectfully requests that the obviousness rejections made under this section be reconsidered and withdrawn.

Based on the foregoing, Applicant believes that the rejections are fully addressed and that the instant claims are now in an allowable condition. A favorable response is earnestly solicited.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. C1037.70048US00.

Dated: August 19, 2009

Respectfully submitted,

By 

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